content we have determined should be useful in understanding the relative reactivities of aldehydic and deoxyribonolactone abasic sites to strand cleavage.

Finally, since ^{17}O NMR chemical shifts are sensitive to hydrogen bonding effects,[7,8,12,13] we anticipate that ^{17}O NMR spectroscopy can also be used as a probe of the accessibility of the abasic site to solvent molecules.

Mechanism of Grignard Reagent Formation. The Surface Nature of the Reaction[1]

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There is a general agreement that the formation of Grignard reagents involve the intermediacy of free radicals.[3-5] The question of whether these radicals are adsorbed on the magnesium surface or diffuse freely in solution has recently been raised by a group of workers[6] who analyze a mechanism ("D-Model") in which the radicals "diffuse freely in solution at all times". The data for the formation of Grignard reagents from *primary alkyl halides* was shown to be consistent with this D model, but herein we show that extrapolation to other substrates may be misleading.

Twenty-seven years ago,[4] it was demonstrated that the reaction of chiral (*S*)-(+)-1-bromo-1-methyl-2,2-diphenylcyclopropane (**1**)
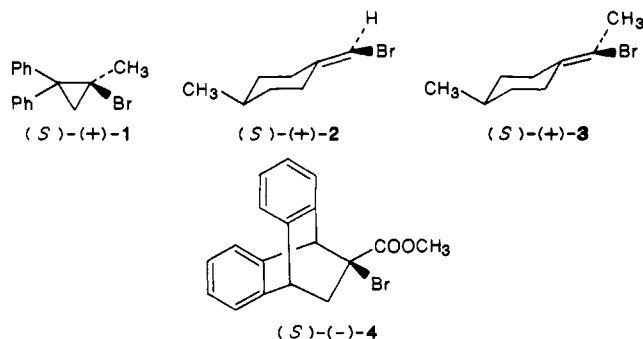
with magnesium powder resulted in the formation of a chiral Grignard reagent which had an optical purity of ca. 12%. It was suggested at the time and later substantiated[7] that the partial racemization observed occurred at the Grignard formation step due to the formation of the 1-methyl-2,2-diphenylcyclopropyl σ radical intermediate. When this same radical is generated *in solution* from a variety of chiral precursors, the resultant products are always racemic,[8] an expected result in view of K. U. Ingold's[9]

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Table I. Reaction of Magnesium in Methanol-*O-d* with R–Br To Yield R–D

R–Br	yield, % R–H + R–D	yield, % R–D	optical purity, %	retentn of configurtn, %
1	87	100[b]	23	72
3[a]	70	93[b,c]	60	80
4[a]	94	95[d]	11	44[e]

[a] The syntheses of these compounds will be reported elsewhere. [b] Determined by using mass spectroscopic analysis, by Prof. Roy King, University of Florida. [c] Minimum value. [d] Determined by NMR, minimum value. [e] Overall inversion as expected, see: Annino, R.; Erickson, R. E.; Michalovic, J.; McKay, B. *J. Am. Chem. Soc.* **1966**, *88*, 4424.

finding that the rate of inversion of the 1-methylcyclopropyl σ radical is on the order of 10^{11} s^{-1} at 71 °C. Only the surface nature of the Grignard formation reaction provides a reasonable explanation for this chirality and for the observation that (*S*)-(+)-4-methylcyclohexylidenebromomethane (**2**) forms a Grignard reagent which is 47% optically pure.[10] Here again, the vinyl σ radical intermediate is reported[11] to invert its configuration between 10^8–10^{10} s^{-1} at −170 °C.

We now wish to report further results of our study designed to help answer the question of whether or not radicals formed during Grignard formation "diffuse freely in solution at all times". It was decided that methanol-*O-d* would be the solvent of choice since, if the radicals left the surface of the magnesium, then the reactive σ radicals formed from the chiral bromides **1**, **3**, and **4** would react with the solvent to abstract a hydrogen atom from the methyl group[12] to yield R–H. If, on the other hand, it was the Grignard reagent that left the surface then it would be quenched by the methanol-*O-d* to give deuterated product R–D. In order to keep the magnesium surface clean and free of magnesium methoxide a continuous stream of carbon dioxide was passed through the reaction mixture[13] to form methyl magnesium carbonate which is soluble in methanol. The reaction of mag-

$$Mg + CH_3OD \rightarrow CH_3OMgD \qquad (1)$$

$$CH_3OMg\text{-}D + CH_3OD \rightarrow (CH_3O)_2Mg + D_2 \qquad (2)$$

$$(CH_3O)_2Mg + 2CO_2 \rightarrow (CH_3OCO_2)_2Mg \qquad (3)$$
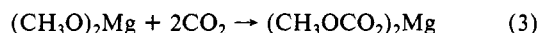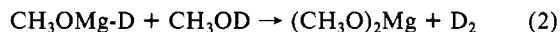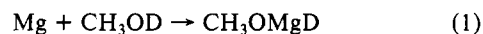
nesium with methanol also produces D_2 which could perhaps reduce the alkyl halide. To check this possibility a reaction was carried out so that a stream of hydrogen as well as the CO_2 was passed through the reaction mixture. The product obtained did not contain any R–H. Finally, consideration was given to the possibility that hydridomagnesium methoxide might be a transient reducing agent.[14] To this end we prepared[15] MgH_2 and to it added a solution of **1** dissolved in methanol. The starting material **1** was recovered unchanged in 98% yield. Thus, we feel confident that we are observing the usual Grignard formation reaction.

As one can see from Table I the yields of R–D are almost quantitative, and the optical purities decrease with decreasing s-character of the orbital involved, **3** > **1** > **4**. Of significance is the observation that **4**, which would give rise to a planar π radical delocalized by an adjacent carbomethoxy group, still yields a product with 11% optical purity. This speaks strongly for an adsorbed radical on the surface of magnesium as does the fact that the rapidly inverting σ radicals **1** and **3** also retain a large

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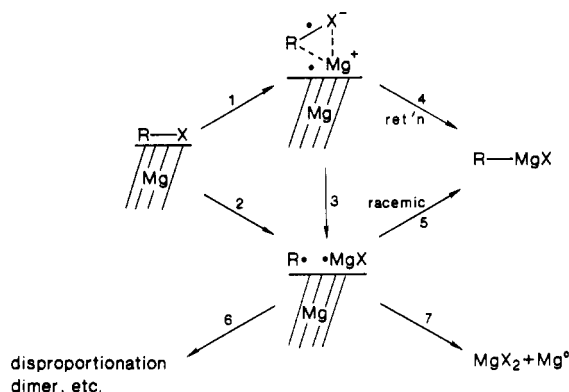(11) Fessenden, R. W.; Schuler, R. H. *J. Chem. Phys.* **1963**, *39*, 2147.

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**Scheme I.** Proposed Mechanism for Grignard Formation

portion of their configuration. It should also be noted that Grignard formations in aprotic solvents give a similar result in that the retention of configuration of **2** (71%)[10] > **1** (59%)[7] > 2-bromooctane (50%; racemization).[16] This is consistent with the observation of Buske and Ford[17] who report that *syn*- and *anti*-7-bromobenzonorbornadiene (the 7-benzonorbornadienyl radical is a σ-radical[18]) yield Grignard reagents with high retention of configuration.

As one might expect the more reactive σ radicals are adsorbed more strongly than π radicals on the magnesium surface. If there is no surface available and the radicals are produced in solution, then the result is complete loss of configuration. Thus, the tri-*n*-butyltin hydride radical chain reductions of **1**, **3**, and **4** gave racemic products, and both *syn*- and *anti*-7-bromobenzonorbornadiene gave an identical mixture of deuterated product when reduced with tri-*n*-butyl deuteride. Since our early work[7] others[17,19-21] have also adopted the radical surface mechanism for Grignard formation which is depicted in Scheme I.

Electron transfer from the magnesium surface into the σ* orbital of the carbon–halogen bond leads to a tightly held anion radical magnesium cation radical pair at the surface where magnesium insertion can occur to produce the Grignard reagent with retention of optical activity and configuration (pathways 1 and 4). If before magnesium insertion, the anion radical magnesium cation radical dissociates at the surface to the radical magnesious halide radical pair, this would, upon recombination, lead, mainly but not exclusively,[22] to the formation of racemic Grignard reagent (pathways 3 and 5). This same radical pair could be formed directly by electron transfer from the surface to the carbon–halogen bond, and the proportion of anion radical magnesium cation formation (pathway 1, retention) vs radical pair formation (pathway 2, largely racemization) would, as observed, be halogen dependent.[4,7,17] Support for the surface nature of the reaction can also be found in the kinetic analysis of the reaction by Molle, Bauer, and Dubois[21] as well as in their XPS studies.[21] The work of Vogler[23] and Whitesides[20] is also consistent with intermediate species such as a radical magnesious halide radical pair (pathway 2) or an anion radical magnesium cation radical adsorbed on the surface of magnesium (pathway 1).

The highly reactive σ radicals will remain largely at the surface, and there they can dimerize or disproportionate (pathway 6) so that in the reaction of **1** in ether[4,7] one observes the formation of **5**, **6**, **7**, and **8**. Of significance is the formation of **8** which is only
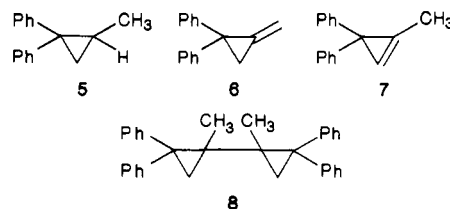
observed in surface[4,7] or surface-like reactions[24] but never when the precursor radical is produced in solution.[25] Compounds **5**, **6**, and **7** are the result of disproportionation of the radical intermediate on the surface.[7] However, some of the radicals leave the surface and react with solvent to form **5**. Using ether-d_{10} as the solvent it was shown that **5** had 6% deuterium incorporated, and in THF-d_8 **5** contained 28% deuterium.[7] Ashby[26] has recently shown that in the reaction of 6-bromo-1-hexene with magnesium, at most, only 25% of the radicals leave the surface.[27] This demonstrates that even a stable π radical remains largely at the surface.

Thus, the evidence that the magnesium surface plays a major role in the Grignard formation reactions is conclusive and is not compatible with intermediate radicals that "diffuse freely in solution at all times".

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(27) This is a minimum value since it assumes 100% efficiency for the radical trapping reagent, DCPH.

Temporal Resolution of the Methylation Sequence of Vitamin B$_{12}$ Biosynthesis

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Previous work from Texas, Stuttgart,[1,2] and Cambridge[3-5] has shown that in the overall conversion of uro'gen III to cobyrinic

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